Hemodialysis failure secondary to hydroxocobalamin exposure

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Hydroxocobalamin is a recently approved antidote for the treatment of cyanide poisoning. The case presented involves a young patient administered empiric hydroxocobalamin due to suspected cyanide overdose. Due to the development of acute kidney injury and severe metabolic derangement, emergent hemodialysis was initiated. Unfortunately, hemodialysis was confounded by a recurrent "blood leak" alarm. This unforeseen effect was secondary to interference from hydroxocobalamin. Hydroxocobalamin causes orange/red discoloration of bodily fluids and permeates the dialysate. This leads to defraction of light in the effluent path of the blood leak detector from discolored dialysate, which can result in activation of the blood leak alarm and an inability to continue hemodialysis treatment. This case highlights several new and emerging critical concerns with this medication, including the potential consequence of delayed initiation of emergent renal replacement therapy with empiric administration, the need for increased awareness among clinicians of various disciplines, and the need for multidisciplinary communication.

Hydroxocobalamin was approved by the Food and Drug Administration in December 2006 for the treatment of cyanide poisoning. For decades, cyanide poisoning has been treated using the cyanide antidote kit (1, 2). This kit contains amyl nitrite, sodium nitrite, and sodium thiosulfate, which can cause hypotension and reduced oxygen-carrying capacity of hemoglobin (3–5). In contrast, hydroxocobalamin does not cause these complications. This property makes it advantageous for patients with already decreased oxygenation, those who have been exposed to carbon monoxide, and pregnant patients. Hydroxocobalamin can therefore be safely used in cases where combined carbon monoxide and cyanide toxicity is suspected. The side-effect profile of hydroxocobalamin is considered minimal compared to its predecessor cyanide antidote kit (6). It can, however, cause orange/red discoloration of skin, blood, urine, and secretions, and this can lead to statistically significant alterations in certain colorimetric tests and co-oximetry measurements (7–9). A newly recognized problem associated with the increasing usage of hydroxocobalamin is the interference of hemodialysis. This is particularly concerning due to the potential ramifications of limiting the provision of life-saving treatment in critically ill intoxicated patients. Here we describe a case of a young patient administered empiric hydroxocobalamin with failure of emergent hemodialysis secondary to interference from hydroxocobalamin.

CASE REPORT

A 24-year-old man with asthma was found unresponsive and profoundly hypotensive by emergency medical services. No eyewitnesses were available. On arrival to the emergency room, he was found in extremis with significant agonal breathing, a Glasgow coma scale score of 3, temperature of 35.3°C, blood pressure of 60/45 mm Hg, heart rate of 74 beats/min, respiratory rate of 24 breaths/min, and cool extremities. His serum creatinine was 1.3 mg/dL; sodium, 145 mmol/L; potassium, 4.6 mmol/L; bicarbonate, 10 mmol/L; anion gap, 39; phosphate, 4.9 mmol/L; lactate, 21.3 mmol/L; and white blood cell count, 27.3 K/uL. A bedside arterial blood gas was significant for a pH of 6.99, a partial pressure of carbon dioxide of 47, and a partial pressure of oxygen of 76. A blood and urine toxicology screen were negative.

Sonography was negative for blunt abdominal trauma. Echocardiogram showed a severely diminished ejection fraction. Radiographs showed mildly increased interstitial markings bilaterally. Despite emergent intubation and intravenous fluid resuscitation, he required rapid escalation to multiple vasopressors. He was administered hydroxocobalamin empirically in the emergency room due to concern for cyanide intoxication. Due to profound acid-base disturbance and concern for intentional overdose, emergent dialysis was initiated using the Fresenius 2008K machine. This was confounded by a recurrent "blood leak alarm" that repeatedly shut down the machine despite a change to a new dialyzer. Emergent salvage extracorporeal membrane oxygenation was commenced, but the patient died. It was later revealed that instead of cyanide, the patient was most likely intoxicated with sodium azide.

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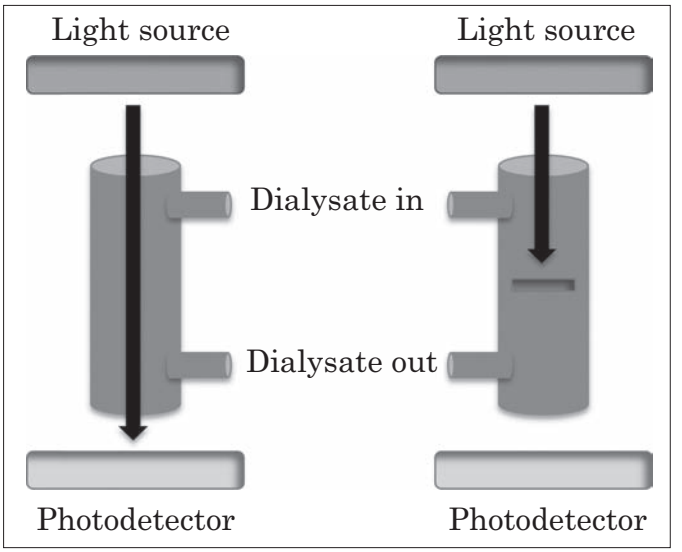

Figure. Diffraction of light in the blood leak detector. Substances that deflect or scatter light, such as hemoglobin or medications causing discoloration of fluids, will result in a loss of transparency at the base of the column, triggering the blood leak detector.

DISCUSSION

There is a severe paucity of data available today to guide the management of hydroxocobalamin use in critically ill patients requiring renal replacement therapy. The case presented here highlights several new and emerging critical concerns with this medication that can impede the delivery of life-saving treatment.

First, while the use of hydroxocobalamin remains an advantage compared to the cyanide antidote kit due to its low toxicity profile, universal discoloration of bodily fluids can impede the delivery of hemodialysis by inducing a "pseudo-blood leak" (10). The hemodialysis machine operates on the principle that blood passes on one side of a semipermeable membrane. An aqueous solution, the dialysate is pumped on the opposite side, typically in the opposite direction of the blood flow, to maximize the diffusion gradient across the membrane. All hemodialysis machines contain a blood leak detector that alarms if red blood cells penetrate into the dialysate *(Figure).* This is a vital safety feature of hemodialysis machines. The blood leak alarm system consists of a photodetector at the bottom of the dialysate column with a light source at the top. Substances that deflect or scatter light such as hemoglobin or medications causing discoloration of fluids will result in a loss of transparency at the base of the column, triggering the blood leak detector (11). Hydroxocobalamin administration results in discoloration of the dialysate and triggers this alarm. Activation of the blood leak detector in the Fresenius 2008K machine causes the blood pump to stop, the venous clamp on the level detector to occlude, the ultrafiltration pump to stop, and the remaining time on dialysis clock to halt (12).

Very limited data are available on the types of dialysis machines that may be affected by hydroxocobalamin. While the Fresenius 2008K hemodialysis machine used in our case can be interfered by hydroxocobalamin, not all types of hemodialysis machines share this property. There is evidence that the Gambro Phoenix X36 and the NxStage machine are unaffected (10, 13). It has been postulated that hemodialysis machines that utilize a photodetector consisting of a single optical emitter designed to detect light scatter and signal drop off are unlikely to be affected by hydroxocobalamin (10). However, photodetectors that use a dual LED array that depends on light absorption, such as those on the Fresenius 2008K, are susceptible to the "pseudo-blood leak" phenomenon.

Another critical concern this case raises is the empiric administration of hydroxocobalamin. An increased awareness of the adverse effects of hydroxocobalamin in patients potentially requiring emergent renal replacement therapy is needed among emergency room physicians, critical care physicians, and nephrologists alike. This will help increase multidisciplinary communication, better inform management decisions and therapeutic options for the critically ill, and help steward dialysis resources. In the case presented, empiric hydroxocobalamin was administered and the patient was eventually found to have not overdosed on cyanide. In another recent case at our institution, a potential kidney donor had received hydroxocobalamin prior to being considered a donor. The transplant team decided to decline the kidney for transplantation in part due to the possibility that intermittent hemodialysis to treat delayed graft function could not be performed due to interference from hydroxocobalamin. While the outcomes of similar scenarios involving transplant donors have not previously been reported, this scenario and the case presented here highlight the critical need for more data to help guide management decisions in patients exposed to hydroxocobalamin requiring renal replacement therapy.

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